

PATENT COOPERATION TREATY

PCT

NOTIFICATION OF ELECTION

(PCT Rule 61.2)

From the INTERNATIONAL BUREAU

To:

Commissioner
 US Department of Commerce
 United States Patent and Trademark
 Office, PCT
 2011 South Clark Place Room
 CP2/5C24
 Arlington, VA 22202
 ETATS-UNIS D'AMERIQUE
 in its capacity as elected Office

Date of mailing (day/month/year) 01 February 2001 (01.02.01)	
International application No. PCT/GB00/01771	Applicant's or agent's file reference IPD/P1235/WOD
International filing date (day/month/year) 09 May 2000 (09.05.00)	Priority date (day/month/year) 13 May 1999 (13.05.99)
Applicant SQUIRRELL, David, James et al	

1. The designated Office is hereby notified of its election made:

☒ in the demand filed with the International Preliminary Examining Authority on:
 22 November 2000 (22.11.00)

☐ in a notice effecting later election filed with the International Bureau on:

2. The election ☒ was
☐ was not

made before the expiration of 19 months from the priority date or, where Rule 32 applies, within the time limit under Rule 32.2(b).

The International Bureau of WIPO 34, chemin des Colombettes 1211 Geneva 20, Switzerland Facsimile No.: (41-22) 740.14.35	Authorized officer Juan Cruz Telephone No.: (41-22) 338.83.38
---	---

PATENT COOPERATION TREATY

PCT

From the INTERNATIONAL BUREAU

NOTIFICATION OF THE RECORDING
OF A CHANGE(PCT Rule 92bis.1 and
Administrative Instructions, Section 422)

To:

BOWDERY, A., O.
D/IPR
Formalities Section
Poplar 2, MOD Abbey Wood #19
Bristol BS34 8JH
ROYAUME-UNI

Date of mailing (day/month/year) 03 juillet 2001 (03.07.01)	IMPORTANT NOTIFICATION
Applicant's or agent's file reference IPD/P1235/WOD	
International application No. PCT/GB00/01771	International filing date (day/month/year) 09 mai 2000 (09.05.00)

1. The following indications appeared on record concerning:

☒ the applicant
 ☐ the inventor
 ☐ the agent
 ☐ the common representative

Name and Address THE SECRETARY OF STATE FOR DEFENCE Defence Evaluation and Research Agency Ively Road Farnborough Hampshire GU14 0LX United Kingdom	State of Nationality GB	State of Residence GB
	Telephone No.	
	Facsimile No.	
	Teleprinter No.	

2. The International Bureau hereby notifies the applicant that the following change has been recorded concerning:

☐ the person
 ☐ the name
 ☒ the address
 ☐ the nationality
 ☐ the residence

Name and Address THE SECRETARY OF STATE FOR DEFENCE CBD Porton Down Salisbury Wiltshire SP4 0JQ United Kingdom	State of Nationality GB	State of Residence GB
	Telephone No.	
	Facsimile No.	
	Teleprinter No.	

3. Further observations, if necessary:

4. A copy of this notification has been sent to:

<input checked="" type="checkbox"/> the receiving Office	<input type="checkbox"/> the designated Offices concerned
<input type="checkbox"/> the International Searching Authority	<input checked="" type="checkbox"/> the elected Offices concerned
<input checked="" type="checkbox"/> the International Preliminary Examining Authority	<input type="checkbox"/> other:

The International Bureau of WIPO 34, chemin des Colombettes 1211 Geneva 20, Switzerland Facsimile No.: (41-22) 740.14.35	Authorized officer Dominique DELMAS Telephone No.: (41-22) 338.83.38
---	--

PATENT COOPERATION TREATY

PCT

From the INTERNATIONAL BUREAU

NOTIFICATION OF THE RECORDING
OF A CHANGE(PCT Rule 92bis.1 and
Administrative Instructions, Section 422)

To:

SKELTON Stephen Richard
D/IPR
Formalities Section
Poplar 2, MOD Abbey Wood #19
Bristol BS34 8JH
ROYAUME-UNI

Date of mailing (day/month/year)
02 August 2001 (02.08.01)

Applicant's or agent's file reference
IPD/P1235/WOD

International application No.
PCT/GB00/01771

IMPORTANT NOTIFICATION

International filing date (day/month/year)
09 May 2000 (09.05.00)

1. The following indications appeared on record concerning:

☒ the applicant ☐ the inventor ☐ the agent ☐ the common representative

Name and Address

THE SECRETARY OF STATE FOR DEFENCE
CBD Porton Down
Salisbury
Wiltshire SP4 0JQ
United Kingdom

State of Nationality
GB

State of Residence
GB

Telephone No.

Facsimile No.

Teleprinter No.

2. The International Bureau hereby notifies the applicant that the following change has been recorded concerning:

☐ the person ☐ the name ☒ the address ☐ the nationality ☐ the residence

Name and Address

THE SECRETARY OF STATE FOR DEFENCE
DSTL Porton Down
Salisbury
Wiltshire SP4 0JQ
United Kingdom

State of Nationality
GB

State of Residence
GB

Telephone No.

Facsimile No.

Teleprinter No.

3. Further observations, if necessary:

4. A copy of this notification has been sent to:

☒ the receiving Office ☐ the designated Offices concerned
☐ the International Searching Authority ☒ the elected Offices concerned
☒ the International Preliminary Examining Authority ☐ other: .

The International Bureau of WIPO
34, chemin des Colombettes
1211 Geneva 20, Switzerland

Authorized officer

HA Ki-Nam

Facsimile No.: (41-22) 740.14.35

Telephone No.: (41-22) 338.83.38

PARENT COOPERATION TREATY

PCT

NOTIFICATION OF THE RECORDING
OF A CHANGE(PCT Rule 92bis.1 and
Administrative Instructions, Section 422)

From the INTERNATIONAL BUREAU

To:

SKELTON Stephen Richard
D/IPR
Formalities Section
Poplar 2, MOD Abbey Wood #19
Bristol BS34 8JH
ROYAUME-UNI

Date of mailing (day/month/year) 30 juillet 2001 (30.07.01)	IMPORTANT NOTIFICATION
Applicant's or agent's file reference IPD/P1235/WOD	
International application No. PCT/GB00/01771	International filing date (day/month/year) 09 mai 2000 (09.05.00)

1. The following indications appeared on record concerning:		
<input type="checkbox"/> the applicant	<input type="checkbox"/> the inventor	<input checked="" type="checkbox"/> the agent
<input type="checkbox"/> the common representative		
Name and Address BOWDERY, A., O. D/IPR Formalities Section Poplar 2, MOD Abbey Wood #19 Bristol BS34 8JH United Kingdom	State of Nationality	State of Residence
	Telephone No. 0117 91 32857	
	Facsimile No. 0117 91 32930	
	Teleprinter No.	
2. The International Bureau hereby notifies the applicant that the following change has been recorded concerning:		
<input type="checkbox"/> the person	<input type="checkbox"/> the name	<input type="checkbox"/> the address
<input type="checkbox"/> the nationality	<input type="checkbox"/> the residence	
Name and Address SKELTON Stephen Richard D/IPR Formalities Section Poplar 2, MOD Abbey Wood #19 Bristol BS34 8JH United Kingdom	State of Nationality	State of Residence
	Telephone No. 0117 91 32857	
	Facsimile No. 0117 91 32930	
	Teleprinter No.	
3. Further observations, if necessary:		
4. A copy of this notification has been sent to:		
<input checked="" type="checkbox"/> the receiving Office	<input type="checkbox"/> the designated Offices concerned	
<input type="checkbox"/> the International Searching Authority	<input checked="" type="checkbox"/> the elected Offices concerned	
<input checked="" type="checkbox"/> the International Preliminary Examining Authority	<input type="checkbox"/> other:	

The International Bureau of WIPO 34, chemin des Colombettes 1211 Geneva 20, Switzerland	Authorized officer HA Ki-Nam
Facsimile No.: (41-22) 740.14.35	Telephone No.: (41-22) 338.83.38

PATENT COOPERATION TREATY

PCT

NOTIFICATION OF THE RECORDING
OF A CHANGE(PCT Rule 92bis.1 and
Administrative Instructions, Section 422)

From the INTERNATIONAL BUREAU

To:

SKELTON Stephen Richard
D/IPR
Formalities Section
Poplar 2, MOD Abbey Wood #19
Bristol BS34 8JH
ROYAUME-UNI

Date of mailing (day/month/year) 31 juillet 2001 (31.07.01)	IMPORTANT NOTIFICATION
Applicant's or agent's file reference IPD/P1235/WOD	
International application No. PCT/GB00/01771	International filing date (day/month/year) 09 mai 2000 (09.05.00)

1. The following indications appeared on record concerning:		
<input checked="" type="checkbox"/> the applicant	<input type="checkbox"/> the inventor	<input type="checkbox"/> the agent
<input type="checkbox"/> the common representative		
Name and Address THE SECRETARY OF STATE FOR DEFENCE CBD Porton Down Salisbury Wiltshire SP4 0JQ United Kingdom	State of Nationality GB	State of Residence GB
	Telephone No.	
	Facsimile No.	
	Teleprinter No.	
2. The International Bureau hereby notifies the applicant that the following change has been recorded concerning:		
<input type="checkbox"/> the person	<input type="checkbox"/> the name	<input checked="" type="checkbox"/> the address
<input type="checkbox"/> the nationality		
<input type="checkbox"/> the residence		
Name and Address THE SECRETARY OF STATE FOR DEFENCE DSTL Porton Down Salisbury Wiltshire SP4 0JQ United Kingdom	State of Nationality GB	State of Residence GB
	Telephone No.	
	Facsimile No.	
	Teleprinter No.	
3. Further observations, if necessary:		
4. A copy of this notification has been sent to:		
<input checked="" type="checkbox"/> the receiving Office	<input type="checkbox"/> the designated Offices concerned	
<input type="checkbox"/> the International Searching Authority	<input checked="" type="checkbox"/> the elected Offices concerned	
<input checked="" type="checkbox"/> the International Preliminary Examining Authority	<input type="checkbox"/> other:	

The International Bureau of WIPO 34, chemin des Colombettes 1211 Geneva 20, Switzerland Facsimile No.: (41-22) 740.14.35	Authorized officer HA Ki-Nam Telephone No.: (41-22) 338.83.38
---	---

FOR THE PURPOSES OF INFORMATION ONLY

Codes used to identify States party to the PCT on the front pages of pamphlets publishing international applications under the PCT.

AL	Albania	ES	Spain	LS	Lesotho	SI	Slovenia
AM	Armenia	FI	Finland	LT	Lithuania	SK	Slovakia
AT	Austria	FR	France	LU	Luxembourg	SN	Senegal
AU	Australia	GA	Gabon	LV	Latvia	SZ	Swaziland
AZ	Azerbaijan	GB	United Kingdom	MC	Monaco	TD	Chad
BA	Bosnia and Herzegovina	GE	Georgia	MD	Republic of Moldova	TG	Togo
BB	Barbados	GH	Ghana	MG	Madagascar	TJ	Tajikistan
BE	Belgium	GN	Guinea	MK	The former Yugoslav Republic of Macedonia	TM	Turkmenistan
BF	Burkina Faso	GR	Greece	ML	Mali	TK	Turkey
BG	Bulgaria	HU	Hungary	MN	Mongolia	TT	Trinidad and Tobago
BJ	Benin	IE	Ireland	MR	Mauritania	UA	Ukraine
BR	Brazil	IL	Israel	MW	Malawi	UG	Uganda
BY	Belarus	IS	Iceland	MX	Mexico	US	United States of America
CA	Canada	IT	Italy	NE	Niger	UZ	Uzbekistan
CF	Central African Republic	JP	Japan	NL	Netherlands	VN	Viet Nam
CG	Congo	KE	Kenya	NO	Norway	YU	Yugoslavia
CH	Switzerland	KC	Kyrgyzstan	NZ	New Zealand	ZW	Zimbabwe
CI	Côte d'Ivoire	KP	Democratic People's Republic of Korea	PL	Poland		
CM	Cameroon	KR	Republic of Korea	PT	Portugal		
CN	China	KZ	Kazakhstan	RO	Romania		
CU	Cuba	LC	Saint Lucia	RU	Russian Federation		
CZ	Czech Republic	LI	Liechtenstein	SD	Sudan		
DE	Germany	LK	Sri Lanka	SE	Sweden		
DK	Denmark	LR	Liberia	SU	Singapore		
EE	Estonia						

INTERNATIONAL SEARCH REPORT

 International Application No
 PCT/GB 00/01771

A. CLASSIFICATION OF SUBJECT MATTER
 IPC 7 C1201/48

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED
 Minimum documentation searched (classification system followed by classification symbols)
 IPC 7 C120

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

EPO-Internal, WPI Data, PAJ, BIOSIS

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	WO 94 17202 A (SECR DEFENCE BRIT ;SQUIRRELL DAVID JAMES (GB)) 4 August 1994 (1994-08-04) cited in the application	1-23
Y	the whole document	1-23
X	WO 96 02665 A (SECR DEFENCE BRIT ;SQUIRRELL DAVID JAMES (GB)) 1 February 1996 (1996-02-01) cited in the application	1-23
Y	the whole document	1-23
X	WO 96 02666 A (SECR DEFENCE ;SQUIRRELL DAVID JAMES (GB)) 1 February 1996 (1996-02-01)	1-23
Y	the whole document	1-23

☒ Further documents are listed in the continuation of box C.

☒ Patent family members are listed in annex.

* Special categories of cited documents:

- "A" document defining the general state of the art which is not considered to be of particular relevance
- "E" earlier document but published on or after the international filing date
- "L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)
- "O" document referring to an oral disclosure, use, exhibition or other means
- "P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art

"Z" document member of the same patent family

Date of the actual completion of the international search

4 September 2000

Date of mailing of the international search report

13/09/2000

Name and mailing address of the ISA

 European Patent Office, P.B. 5618 Patendaan 2
 NL - 2280 HV Rijswijk
 Tel (+31-70) 340-3040, Tx 31 651 epo nl,
 Fax (+31-70) 340-3016

Authorized officer

Pellegrini, P

Form PCT/ISA/210 (second sheet) (July 1992)

INTERNATIONAL SEARCH REPORT

International Application No
PCT/GB 00/01771

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	EP 0 376 189 A (YEDA RES & DEV) 4 July 1990 (1990-07-04) claim 1	1-23
P, X	WO 99 37799 A (MURPHY MELANIE JANE ; PRICE RACHEL LOUISE (GB); SQUIRRELL DAVID JAM) 29 July 1999 (1999-07-29)	1-23
P, Y	the whole document	1-23

Form PCT/ISA/210 (continuation of second sheet) (July 1992)

page 2 of 2

06 NOV 2001 10:50

+44 1980 613529

PAGE.22

11/07/01 WED 07:06 [TX/RX NO 7310]

INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No.

PCT/GB 00/01771

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
WO 9417202 A	04-08-1994	AT 170222 T	15-09-1998
		AU 677627 B	01-05-1997
		AU 5841794 A	15-08-1994
		BR 9406417 A	26-12-1995
		CA 2154462 A	04-08-1994
		CN 1119029 A	20-03-1996
		DE 69412790 D	01-10-1998
		DE 69412790 T	11-02-1999
		EP 0680515 A	08-11-1995
		ES 2120006 T	16-10-1998
		GB 2289945 A, B	06-12-1995
		HU 72396 A	29-04-1996
		NO 952917 A	06-09-1995
		NZ 259576 A	24-06-1997
		US 5648232 A	15-07-1997
WO 9602665 A	01-02-1996	AU 698916 B	12-11-1998
		AU 7130594 A	16-02-1996
		BR 9408598 A	18-11-1997
		EP 0788553 A	13-08-1997
		GB 2303919 A, B	05-03-1997
		JP 10502538 T	10-03-1998
		NO 970105 A	13-03-1997
		NZ 268405 A	19-12-1997
WO 9602666 A	01-02-1996	AT 184054 T	15-09-1999
		AU 691940 B	28-05-1998
		AU 2931995 A	16-02-1996
		BR 9508392 A	26-05-1998
		CA 2194458 A	01-02-1996
		CN 1157638 A	20-08-1997
		DE 69511876 D	07-10-1999
		DE 69511876 T	31-05-2000
		EP 0774011 A	21-05-1997
		ES 2136866 T	01-12-1999
		GB 2304892 A, B	26-03-1997
		HU 76447 A	29-09-1997
		JP 10502815 T	17-03-1998
		NO 970106 A	13-03-1997
		NZ 289464 A	28-07-1998
		US 5798214 A	25-08-1998
		ZA 9505846 A	19-02-1996
EP 0376189 A	04-07-1990	US 5215888 A	01-06-1993
WO 9937799 A	29-07-1999	AU 2065399 A	09-08-1999

Form PCT/ISA/210 (patent family annex) (July 1992)

REPLACED BY
ART 34 AMDT

WO 00/70082

PCT/GB00/01771

14

Claims

1. A method for detecting the presence of a lysed eukaryotic cell in a sample, said method comprising
 - 5 (i) adding adenosine diphosphate (ADP) to said sample under conditions which allows the conversion of ADP to adenosine triphosphate (ATP) by cellular adenylate kinase,
 - (ii) detecting ATP in said sample and relating that to the presence of adenylate kinase and thus to the presence of
 - 10 lysed cells.
2. A method according to claim 1 for use in monitoring cell integrity in a cell preparation.
- 15 3. A method according to claim 2 wherein the cell preparation is subjected to test conditions which are suspected of causing cell lysis.
4. A method according to claim 6 wherein the said test
- 20 conditions comprise addition of a reagent.
5. A method according to claim 4 wherein the said reagent is a compound which is being screened for pharmaceutical application.
- 25 6. A method according to claim 5 wherein the cell preparation is a tumour cell line in culture medium and the reagent is suspected of having anti-cancer applications.
- 30 7. A method according to claim 3 wherein the said test conditions comprise variation in an environmental factor.
8. A method according to claim 7 wherein the said environmental factor is temperature, pH, pressure,
- 35 irradiation or the presence of a particular gaseous environment.

WO 00/70082

PCT/GB00/01771

15

9. A method according to claim 1 which is used to diagnose infection of the cells by a lytic virus.
10. A method according to any one of the preceding claims
3 which is used in toxicity testing.
11. A method according to claim 1 which is used to monitor the condition of eukaryotic cells in a sample, wherein cells which have been incubated under test conditions are lysed, in
10 a preliminary step, and thereafter the quantity of ATP detected is used to determine the condition of the cells.
12. A method according to claim 11 wherein the sample contains a known amount of cells, and is cultured prior to
15 said preliminary step under test conditions which are suspected of affecting the condition of the cells.
13. A method according to claim 12 wherein the said test conditions comprise addition of a reagent.
20
14. A method according to claim 13 wherein the said reagent is a compound which is being screened for growth factor activity.
- 25 15. A method according to claim 3 wherein the said test conditions comprise variation in an environmental factor.
16. A method according to claim 15 wherein the said environmental factor is temperature, pH, pressure,
30 irradiation or the presence of a particular gaseous environment.
17. A method according to claim 1 which is used to detect the presence of eukaryotic cells in a sample wherein, in a
35 preliminary step, cells in the sample are lysed.

WO 00/70082

PCT/GB00/01771

16

18. A method according to claim 17 wherein the sample is a sample of urine or milk.
19. A method according to claim 18 which is used to diagnose the presence of a disease state in the animal providing the said sample.
20. A method according to any one of claims 11 to 19, wherein in a preliminary step, the cells are lysed by addition of a lytic agent.
21. A test kit for effecting a method according to claim 1, which comprises substantially pure ADP, detection reagents and cell culture medium.
22. A test kit according to claim 21 wherein the detection reagents are luciferase/luciferin which is substantially free of contaminating enzymes.
23. A method for detecting the presence of lysed eukaryotic cells substantially as herein before described.

IPR1 RECEIVED

From the
INTERNATIONAL PRELIMINARY EXAMINING AUTHORITY

PCT

23 JUL 2001

MOD-DPA

NOTIFICATION OF TRANSMITTAL OF
THE INTERNATIONAL PRELIMINARY
EXAMINATION REPORT
(PCT Rule 71.1)

To:

SKELTON, Stephen Richard
D/IPR Formalities
Poplar 2a
MOD Abbey Wood 19
Bristol BS34 8JH
GRANDE BRETAGNEDate of mailing
(day/month/year)

18.07.2001

Applicant's or agent's file reference
IPD/P1235/WOD

IMPORTANT NOTIFICATION

International application No.
PCT/GB00/01771International filing date (day/month/year)
09/05/2000Priority date (day/month/year)
13/05/1999

Applicant

THE SECRETARY OF STATE FOR DEFENCE et al.

1. The applicant is hereby notified that this International Preliminary Examining Authority transmits herewith the international preliminary examination report and its annexes, if any, established on the international application.
2. A copy of the report and its annexes, if any, is being transmitted to the International Bureau for communication to all the elected Offices.
3. Where required by any of the elected Offices, the International Bureau will prepare an English translation of the report (but not of any annexes) and will transmit such translation to those Offices.

4. REMINDER

The applicant must enter the national phase before each elected Office by performing certain acts (filing translations and paying national fees) within 30 months from the priority date (or later in some Offices) (Article 39(1)) (see also the reminder sent by the International Bureau with Form PCT/IB/301).

Where a translation of the international application must be furnished to an elected Office, that translation must contain a translation of any annexes to the international preliminary examination report. It is the applicant's responsibility to prepare and furnish such translation directly to each elected Office concerned.

For further details on the applicable time limits and requirements of the elected Offices, see Volume II of the PCT Applicant's Guide.

Name and mailing address of the IPEA/



European Patent Office
D-80298 Munich
Tel. +49 89 2399 - 0 Tx: 523656 epmu d
Fax: +49 89 2399 - 4465

Authorized officer

Danti, B

Tel. +49 89 2399-8161





Form PCT/IPEA/416 (July 1992)

PATENT COOPERATION TREATY

PCT

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference IPD/P1235/WOD		FOR FURTHER ACTION See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/416)	
International application No. PCT/GB00/01771	International filing date (day/month/year) 09/05/2000	Priority date (day/month/year) 13/05/1999	
International Patent Classification (IPC) or national classification and IPC C12Q1/48			
Applicant THE SECRETARY OF STATE FOR DEFENCE et al.			
<p>1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.</p> <p>2. This REPORT consists of a total of 5 sheets, including this cover sheet.</p> <p><input checked="" type="checkbox"/> This report is also accompanied by ANNEXES, i.e. sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).</p> <p>These annexes consist of a total of 3 sheets.</p>			
<p>3. This report contains indications relating to the following items:</p> <p>I <input checked="" type="checkbox"/> Basis of the report</p> <p>II <input type="checkbox"/> Priority</p> <p>III <input type="checkbox"/> Non-establishment of opinion with regard to novelty, inventive step and industrial applicability</p> <p>IV <input type="checkbox"/> Lack of unity of invention</p> <p>V <input checked="" type="checkbox"/> Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement</p> <p>VI <input type="checkbox"/> Certain documents cited</p> <p>VII <input type="checkbox"/> Certain defects in the international application</p> <p>VIII <input checked="" type="checkbox"/> Certain observations on the international application</p>			
Date of submission of the demand 22/11/2000		Date of completion of this report 18.07.2001	
Name and mailing address of the international preliminary examining authority:  European Patent Office D-80298 Munich Tel. +49 89 2399 - 0 Tx: 523656 epmu d Fax: +49 89 2399 - 4465		Authorized officer Hinchliffe, P Telephone No. +49 89 2398 8431 	

Form PCT/IPEA/409 (cover sheet) (January 1994)

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No. PCT/GB00/01771

I. Basis of the report

1. With regard to the elements of the international application (*Replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report since they do not contain amendments (Rules 70.16 and 70.17):* Description, pages:

1-13 as originally filed

Claims, No.:

1-23 as received on 08/05/2001 with letter of 08/05/2001

2. With regard to the language, all the elements marked above were available or furnished to this Authority in the language in which the international application was filed, unless otherwise indicated under this item.

These elements were available or furnished to this Authority in the following language: . which is:

- ☐ the language of a translation furnished for the purposes of the international search (under Rule 23.1(b)).
 - ☐ the language of publication of the international application (under Rule 48.3(b)).
 - ☐ the language of a translation furnished for the purposes of international preliminary examination (under Rule 55.2 and/or 55.3).
3. With regard to any nucleotide and/or amino acid sequence disclosed in the international application, the international preliminary examination was carried out on the basis of the sequence listing:
- ☐ contained in the international application in written form.
 - ☐ filed together with the international application in computer readable form.
 - ☐ furnished subsequently to this Authority in written form.
 - ☐ furnished subsequently to this Authority in computer readable form.
 - ☐ The statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.
 - ☐ The statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished.

4. The amendments have resulted in the cancellation of:

- ☐ the description, pages:
- ☐ the claims, Nos.:
- ☐ the drawings, sheets:

5. ☐ This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed (Rule 70.2(c)):

**INTERNATIONAL PRELIMINARY
EXAMINATION REPORT**

International application No. PCT/GB00/01771

(Any replacement sheet containing such amendments must be referred to under item 1 and annexed to this report.)

6. Additional observations, if necessary:

V. Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Yes: Claims 1-23
	No: Claims
Inventive step (IS)	Yes: Claims
	No: Claims 1-23
Industrial applicability (IA)	Yes: Claims 1-23
	No: Claims

2. Citations and explanations
see separate sheet

VIII. Certain observations on the international application

The following observations on the clarity of the claims, description, and drawings or on the question whether the claims are fully supported by the description, are made:
see separate sheet

**INTERNATIONAL PRELIMINARY
EXAMINATION REPORT - SEPARATE SHEET**

International application No. PCT/GB00/01771

ITEM V

1. The priority document of the present application was available at the time that this report was written. Consequently the document cited as P'X' in the I.S.R. is not relevant to the question of novelty of the claims.

2. The subject matter of claims 1-23 is not considered to involve an inventive step contrary to Article 33(3) PCT.

The problem to be solved is that of assaying the effect of certain conditions upon cell intactness. The conditions envisaged are numerous and involve addition of agents which are cytotoxic, effects of lytic viruses and physical conditions. D4 (as cited in the ISR) is considered to represent the closest state of the art as it provides a method and kit for assaying cellular integrity of blood platelets. The assay is also suggested for use in testing out pharmaceutical compositions which effect cellular integrity (see introduction). D4 and the present application thus both propose assays for testing cellular integrity. However D4 tests for the release of PKA whilst the present application tests for the enzyme released by loss of cell integrity, adenylate cyclase. D2 (as cited in the ISR) notes the following in its conclusions on p. 16:

"Thus for a given microorganism [*including eukaryotic cells such as yeasts*] a particular calibration curve may be required, and it may be necessary to provide such curves for different states of the same microorganism, eg. for weakened, pH or oxygen stressed organisms"

D2 is concerned with the same assay as currently envisaged and notes (as shown above) that this assay may be used to detect the effects of i.a. environmental factors on cells. Therefore the skilled person is aware from D2, alone, that physical factors may effect the adenylate kinase present in a sample of microorganisms. Therefore the deliberate use of the method of D2 to test for the effects of environmental factors as well as drugs (as in D4) on the cell integrity and release of adenylate kinase is obvious to the skilled person. Consequently no inventive step can be seen for the subject matter of these claims.

3. The kits covered by claims 21 and 22 differ over those of D1 to D3 by the inclusion of a cell culture reagent in addition to luciferin/luciferase and pure ADP components. Whilst this difference assures novelty over these documents (Article

**INTERNATIONAL PRELIMINARY
EXAMINATION REPORT - SEPARATE SHEET**

International application No. PCT/GB00/01771

33(2) PCT, it is doubtful if this component solves any problem in an inventive manner. The addition of a culture medium is regarded as trivial insofar as the samples may already be in a culture media. Consequently providing a culture medium does not add anything surprising to what is an already known kit (see D1 to D3) and consequently an additional objection under Article 33(3) is made to the subject matter of these two claims.

ITEM VIII

4. The term "particular conditions", found in claim 1, is unclear and leaves the reader in doubt as to exactly what is meant. Consequently claim 1 is contrary to the requirements of Article 6 PCT.
5. Claim 23 is unclear contrary to Article 6 PCT because the term "herein before described" does not provide a clearly delineated subject matter seeking patent protection.

14

Claims

1. A method for monitoring eukaryotic cell integrity under particular conditions, said method comprising
 - (i) subjecting cells to said conditions,
 - (ii) adding adenosine diphosphate (ADP) to said sample under conditions which allow the conversion of ADP to adenosine triphosphate (ATP) by cellular adenylate kinase,
 - (iii) detecting ATP in said sample and relating that to the presence of adenylate kinase and thus to the presence of lysed cells.
2. A method according to claim 1 wherein the conditions are those encountered during storage of a cell preparation.
3. A method according to claim 1 wherein in step (i), the cells are subjected to test conditions which are suspected of causing cell lysis.
4. A method according to claim 3 wherein the said test conditions comprise addition of a reagent.
5. A method according to claim 4 wherein the said reagent is a compound which is being screened for pharmaceutical application.
6. A method according to claim 5 wherein the cell preparation is a tumour cell line in culture medium and the reagent is suspected of having anti-cancer applications.
7. A method according to claim 3 wherein the said test conditions comprise variation in an environmental factor.
8. A method according to claim 7 wherein the said environmental factor is temperature, pH, pressure, irradiation or the presence of a particular gaseous environment.

EMPFANGSZEIT: 8. MAI. 15:37

06 NOV 2001 10:40

AMENDED SHEET

00000000000000000000

+44 1980 613529

PAGE.15

11/07/01 WED 07:06 [TX/RX NO 7310]

1.5

10. A method according to any one of the preceding claims which
5 is used in toxicity testing.

10 5 A method according to claim 1 which is used to monitor the condition of eukaryotic cells in a sample, wherein after step (i) and prior to step (ii), cells which have been incubated under test conditions are lysed, and thereafter the quantity of ATP detected is used to determine the condition of the cells.

12. A method according to claim 11 wherein the sample contains a known amount of cells, and in step (1), it is cultured under test conditions which are suspected of affecting the condition of the cells.

13. A method according to claim 12 wherein the said test conditions comprise addition of a reagent.

14. A method according to claim 13 wherein the said reagent is a compound which is being screened for growth factor activity.

15. A method according to claim 3 wherein the said test conditions comprise variation in an environmental factor.

16. A method according to claim 15 wherein the said environmental factor is temperature, pH, pressure, irradiation or the presence of a particular gaseous environment.

17. A method according to claim 1 which is used to detect the presence of eukaryotic cells in a sample wherein, prior to step (ii), cells in the sample are lysed.

EMPFANGSZEIT: 8. MAI. 15:37

AMENDED SHEET

06 NOV 2001 10:40

11/07/01 WED 07:06 [TX/RX NO 7310] PAGE 16

08-05-2001

16

18. A method according to claim 17 wherein the sample is a sample of urine or milk.

19. A method according to claim 18 which is used to diagnose the presence of a disease state in the animal providing the said sample.

20. A method according to any one of claims 11 to 19, the cells are lysed by addition of a lytic agent.

21. A test kit for effecting a method according to claim 1, which comprises substantially pure ADP, detection reagents and cell culture medium.

22. A test kit according to claim 21 wherein the detection reagents are luciferase/luciferin which is substantially free of contaminating enzymes.

23. A method for detecting the presence of lysed eukaryotic cells substantially as herein before described.

AMENDED SHEET

06 NOV 2001 10:40

+44 1990 613529

TOTAL P.17
PAGE 17

11/07/01 WED 07:06 [TX/RX NO 7310]

INTERNATIONAL COOPERATION TREATY

PCT

INTERNATIONAL SEARCH REPORT

(PCT Article 18 and Rules 43 and 44)

Applicant's or agent's file reference IPD/P1235/WOD	FOR FURTHER ACTION see Notification of Transmittal of International Search Report (Form PCT/ISA/220) as well as, where applicable, item 5 below.	
International application No. PCT/GB 00/ 01771	International filing date (day/month/year) 09/05/2000	(Earliest) Priority Date (day/month/year) 13/05/1999
Applicant THE SECRETARY OF STATE FOR DEFENCE		

This International Search Report has been prepared by this International Searching Authority and is transmitted to the applicant according to Article 18. A copy is being transmitted to the International Bureau.

This International Search Report consists of a total of 3 sheets.
☒ It is also accompanied by a copy of each prior art document cited in this report.

1. Basis of the report

a. With regard to the **language**, the international search was carried out on the basis of the international application in the language in which it was filed, unless otherwise indicated under this item.

☐ the international search was carried out on the basis of a translation of the international application furnished to this Authority (Rule 23.1(b)).

b. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international search was carried out on the basis of the sequence listing :

☐ contained in the international application in written form.

☐ filed together with the international application in computer readable form.

☐ furnished subsequently to this Authority in written form.

☐ furnished subsequently to this Authority in computer readable form.

☐ the statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.

☐ the statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished

2. ☐ **Certain claims were found unsearchable** (See Box I).

3. ☐ **Unity of Invention is lacking** (see Box II).

4. With regard to the **title**,

☒ the text is approved as submitted by the applicant.

☐ the text has been established by this Authority to read as follows:

5. With regard to the **abstract**,

☒ the text is approved as submitted by the applicant.

☐ the text has been established, according to Rule 38.2(b), by this Authority as it appears in Box III. The applicant may, within one month from the date of mailing of this international search report, submit comments to this Authority.

6. The figure of the **drawings** to be published with the abstract is Figure No.

☐ as suggested by the applicant.

☐ because the applicant failed to suggest a figure.

☐ because this figure better characterizes the invention.

☐ None of the figures.

INTERNATIONAL SEARCH REPORT

International Application No

PCT/GB 00/01771

A. CLASSIFICATION OF SUBJECT MATTER

IPC 7 C12Q1/48

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

IPC 7 C12Q

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

EPO-Internal, WPI Data, PAJ, BIOSIS

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	WO 94 17202 A (SECR DEFENCE BRIT ;SQUIRRELL DAVID JAMES (GB)) 4 August 1994 (1994-08-04) cited in the application the whole document	1-23
Y	---	1-23
X	WO 96 02665 A (SECR DEFENCE BRIT ;SQUIRRELL DAVID JAMES (GB)) 1 February 1996 (1996-02-01) cited in the application the whole document	1-23
Y	---	1-23
X	WO 96 02666 A (SECR DEFENCE ;SQUIRRELL DAVID JAMES (GB)) 1 February 1996 (1996-02-01) the whole document	1-23
Y	---	1-23
	--- -/--	



Further documents are listed in the continuation of box C.



Patent family members are listed in annex.

* Special categories of cited documents :

"A" document defining the general state of the art which is not considered to be of particular relevance

"E" earlier document but published on or after the international filing date

"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.

"&" document member of the same patent family

Date of the actual completion of the international search

4 September 2000

Date of mailing of the international search report

13/09/2000

Name and mailing address of the ISA

European Patent Office, P.B. 5818 Patentaan 2
NL - 2280 HV Rijswijk
Tel. (+31-70) 340-2040, Tx. 31 651 epo nl,
Fax: (+31-70) 340-3016

Authorized officer

Pellegrini, P

INTERNATIONAL SEARCH REPORT

International Application No

PCT/GB 00/01771

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	EP 0 376 189 A (YEDA RES & DEV) 4 July 1990 (1990-07-04) claim 1 -----	1-23
P,X	WO 99 37799 A (MURPHY MELANIE JANE ;PRICE RACHEL LOUISE (GB); SQUIRRELL DAVID JAM) 29 July 1999 (1999-07-29)	1-23
P,Y	the whole document -----	1-23

INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No

PCT/GB 00/01771

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
WO 9417202 A	04-08-1994	AT 170222 T AU 677627 B AU 5841794 A BR 9406417 A CA 2154462 A CN 1119029 A DE 69412790 D DE 69412790 T EP 0680515 A ES 2120006 T GB 2289945 A, B HU 72396 A NO 952917 A NZ 259576 A US 5648232 A	15-09-1998 01-05-1997 15-08-1994 26-12-1995 04-08-1994 20-03-1996 01-10-1998 11-02-1999 08-11-1995 16-10-1998 06-12-1995 29-04-1996 06-09-1995 24-06-1997 15-07-1997
WO 9602665 A	01-02-1996	AU 698916 B AU 7130594 A BR 9408598 A EP 0788553 A GB 2303919 A, B JP 10502538 T NO 970105 A NZ 268405 A	12-11-1998 16-02-1996 18-11-1997 13-08-1997 05-03-1997 10-03-1998 13-03-1997 19-12-1997
WO 9602666 A	01-02-1996	AT 184054 T AU 691940 B AU 2931995 A BR 9508392 A CA 2194458 A CN 1157638 A DE 69511876 D DE 69511876 T EP 0774011 A ES 2136866 T GB 2304892 A, B HU 76447 A JP 10502815 T NO 970106 A NZ 289464 A US 5798214 A ZA 9505846 A	15-09-1999 28-05-1998 16-02-1996 26-05-1998 01-02-1996 20-08-1997 07-10-1999 31-05-2000 21-05-1997 01-12-1999 26-03-1997 29-09-1997 17-03-1998 13-03-1997 28-07-1998 25-08-1998 19-02-1996
EP 0376189 A	04-07-1990	US 5215888 A	01-06-1993
WO 9937799 A	29-07-1999	AU 2065399 A	09-08-1999